Amendment to the Claims:

This listing of claims will replace all prior versions, and listings, of the claims in the application.

Listing of Claims:

Claim 1 (currently amended): A method for delivery of a therapeutic or diagnostic agent, the method comprising:

administering a fluid comprising a therapeutic or diagnostic agent to a preselected region within an organ, by forming a substantially closed chamber within or adjacent the organ, and delivering the fluid at a preselected pressure, flow rate or volume of administration to direct delivery of the fluid to the preselected region wherein the therapeutic or diagnostic agent is administered via the device of claim 61.

Claim 2 (original): The method of claim 1, wherein the preselected region is a histological layer of the organ.

Claim 3 (original): The method of claim 2, wherein the histological layer is selected from the group consisting of (a) an epithelial or subepithelial layer; (b) an endothelial or subendothelial layer; (c) a serosa or subserosal layer; and (d) an adventitial or subadventitial layer.

Claim 4 (original): The method of claim 1, wherein the organ comprises a blood vessel or a hollow viscus, and an interior volume of the blood vessel or hollow viscus is isolated to control the predetermined pressure, flow rate or volume of administration.

Claim 5 (original): The method of claim 1, wherein an external area of the organ is isolated to control the preselected pressure, flow rate, or volume of administration.

Claim 6 (original): The method of claim 1 further comprising:

forming a closed chamber within the organ by forming a closed chamber within a hollow organ space within the organ or forming a closed chamber around the organ or a portion of the organ; and

administering the fluid into the hollow organ space or the chamber around the organ; and

controlling at least one of a pressure, a flow rate, and a volume of the administration of the fluid in the closed chamber such that the agent is selectively delivered either to a region deep to a superficial layer, or substantially only to a superficial layer surrounding the hollow organ space, or is selectively delivered to the external surface of the organ, or substantially only to a layer deep to the external surface of the organ.

Claim 7 (original): The method of claim 1 wherein controlling at least one of the pressure, the flow rate, and the volume comprises determining a threshold pressure for disruption of microanatomic barriers that inhibit subepithelial delivery of the agent, and (a) administering the fluid at a pressure below the threshold pressure when delivery only to the superficial layer is desired, or (b) administering the fluid at a pressure at or above the threshold pressure when delivery to the region deep to the superficial layer is desired.

Claim 8 (original): The method of claim 1, wherein controlling at least one of the pressure, the flow rate, and the volume comprises controlling a liquid pressure.

Claim 9 (original): The method of claim 8, wherein controlling the liquid pressure comprises controlling a pressure gradient within or across the organ.

Claim 10 (original): The method of claim 8, wherein controlling the liquid pressure comprises administering the liquid at a constant pressure.

Claim 11 (original): The method of claim 1, wherein forming a closed chamber within a hollow organ space comprises accessing the hollow organ space, substantially occluding an outlet therefrom, and draining the hollow organ space to remove bodily fluids that may interfere with the action of the therapeutic or diagnostic agent.

Claim 12 (original): The method of claim 11 further comprising, after draining the hollow organ space, rinsing the hollow organ space so as to remove traces of bodily fluids that may interfere with the action of the therapeutic or diagnostic agent.

Claim 13 (original): The method of claim 6, further comprising, after administering the fluid comprising the therapeutic or diagnostic agent, draining the hollow organ space to remove the agent.

Claim 14 (original): The method of claim 13, further comprising, after draining the hollow organ space to remove the therapeutic or diagnostic agent, rinsing the hollow organ space to remove traces of the agent.

Claim 15 (original): The method of claim 6 wherein the superficial layer consists of epithelial cells surrounding the hollow organ space and the area deep to the superficial layer consists of areas deep to said epithelial cells.

Claim 16 (original): The method of claim 1 wherein controlling at least one of the pressure, the flow rate, and the volume comprises substantially occluding an outlet from a hollow organ space, and varying the flow rate or volume so as to obtain a desired pressure.

Claim 17 (original): The method of claim 1 wherein controlling at least one of the pressure, the flow rate, and the volume comprising administering a specified volume in a closed chamber.

Claim 18 (original): The method of claim 1, further comprising predetermining a threshold pressure, flow rate or volume for delivery to a selected anatomic or microanatomic site, and controlling at least one of a pressure, flow rate or volume to direct delivery of the agent to the selected site.

Claim 19 (original): The method of claim 18 wherein predetermining a threshold further comprises administering a test fluid into the closed chamber at a given flow rate and measuring a peak pressure at which delivery to a region deep to the superficial layer commences, and wherein controlling at least one of the pressure, the flow rate or the volume comprises administering the fluid (1) as part of a fluid flow into the closed chamber during which the peak pressure is not exceeded, when selective delivery only to a superficial layer is desired, or (2) as part of a fluid flow into the closed chamber during which the peak pressure is equaled or exceeded, when selective delivery to a region deep to the superficial layer is desired.

Claim 20 (original): The method of claim 1 further comprising administering a test fluid into the hollow organ space multiple times, at a given flow rate, and measuring respective multiple peak pressures at which delivery to a region deep to the superficial layer commences, and wherein controlling at least one of the pressure, the flow rate, and the volume comprises administering the fluid comprising the therapeutic or diagnostic agent (1) as part of a fluid flow during which the last-measured peak is not exceeded, when selective delivery only to a superficial layer is desired, or (2) as part of a fluid flow during which the last-measured peak pressure is equaled or exceeded, when selective delivery to a region deep to the superficial layer is desired.

Claim 21 (original): The method of claim 1 wherein the closed chamber comprises a hollow organ space, and controlling at least one of the pressure, the flow rate, and the volume comprises administering the fluid comprising the therapeutic or diagnostic agent at a pressure only slightly above a normal physiologic intralumenal pressure in the hollow organ space, at a pressure sufficient to achieve selective delivery substantially only to the superficial layer.

Claim 22 (original): The method of claim 21 wherein the fluid administered slightly above a normal physiologic intralumenal pressure is administered at a pressure no more than about 2-5 mg Hg above the normal physiologic intralumenal pressure in the hollow organ space.

Claim 23 (original): The method of claim 6 wherein the hollow organ space comprises a non-vascular interior of a hollow viscus.

Claim 24 (original): The method of claim 6 wherein the hollow organ space comprises the lumen of a duct.

Claim 25 (original): The method of claim 1 wherein the closed chamber comprises a hollow organ space, and the method further comprises isolating a portion of the hollow organ space within the body to form the substantially closed chamber.

Claim 26 (original): The method of claim 25 wherein isolating the portion of the hollow organ space comprises occluding a duct draining the organ.

Claim 27 (original): The method of claim 26 wherein the isolated portion of the hollow organ space comprises the hepatobiliary tract.

Claim 28 (original): The method of claim 25 wherein the isolated portion of the hollow organ space comprises the gall bladder and/or ducts of the hepatobiliary tract.

Claim 29 (original): The method of claim 25 wherein the isolated portion of the hollow organ space comprises hepatic bile ducts or at least a portion of intestine.

Claim 30 (original): The method of claim 7 wherein controlling at least one of the pressure, the flow rate and the volume comprises administering the fluid above the threshold pressure to the region deep to the superficial layer.

Claim 31 (original): The method of claim 20 wherein the fluid is administered above the threshold pressure, at a sufficient pressure to drive the therapeutic or diagnostic agent into a parenchyma of the organ.

Claim 32 (original): The method of claim 25 wherein the pressure drives the therapeutic or diagnostic agent into the parenchyma of the liver.

Claim 33 (original): The method of claim 1 wherein the therapeutic or diagnostic agent comprises at least one of a chemotherapy agent, a pro-inflammatory agent, an anti-inflammatory agent, and a genetic vector.

Claim 34 (original): The method of claim 6 wherein the therapeutic or diagnostic agent comprises a genetic vector, and at least one of a pressure, a flow rate, and a volume of the administration of the fluid is controlled such that selective delivery of the genetic vector is made substantially only to superficial cells adjoining the hollow organ space.

Claim 35 (original): The method of claim 6 wherein the hollow organ space comprises at least a portion of the hepatobiliary tract, the therapeutic or diagnostic agent comprises a genetic vector, and at least one of a pressure, a flow rate, and a volume of the administration of the fluid is controlled such that selective delivery is made to hepatocytes near the hollow organ space.

Claim 36 (original): The method of claim 6 wherein the hollow organ space is in an organ that includes a neoplasm, and the agent comprises an anti-neoplastic agent or a pro-inflammatory cytokine.

Claim 37 (currently amended): The method of claim 6 wherein the hollow organ space comprises:

(a) a portion of the hepatobiliary system adjacent to or involved with hepatic fibrosis, primary biliary cirrhosis or sclerosing cholangitis, and the therapeutic or diagnostic agent comprises an anti-inflammatory agent; or

(b) a portion of intestine affected with Crohn's disease, and the therapeutic or diagnostic agent comprises an anti-inflammatory agent for delivery at a sufficient pressure to introduce the therapeutic or diagnostic agent to a subepithelial lamina propria of the intestinal wall; or

(c) a portion of hepatobiliary tract, the superficial layer comprises epithelial cells lining the hepatobiliary tract, and the region deep to the superficial layer comprises at least one of sinusoids of the liver, Space of Disse, lamina propria, and smooth muscle cells of the gall bladder; or

(d) a portion of the pancreas affected by pancreatic adenocarcinoma and the ~~the~~ therapeutic agent comprises an anti-neoplastic agent or a pro-inflammatory agent or an agent that promotes the formation of blood vessels; and the agent is delivered to either the epithelial cells or subepithelial cells or both; or

(e) a portion of the esophagus affected by esophageal carcinoma and the therapeutic agent comprises an anti-neoplastic agent or a pro-inflammatory agent; or

(f) a portion of the prostate gland affected by prostatic carcinoma and the therapeutic agent comprises an anti-neoplastic agent or a pro-inflammatory agent; or

(g) a portion of the urinary bladder affected by carcinoma and the therapeutic agent comprises an anti-neoplastic agent or a pro-inflammatory agent delivered to either the superficial epithelial cells, the lamina propria, any or all of the circular and longitudinal muscle layers, and/or the serosa.

Claim 38 (original): The method of claim 1, wherein the agent comprises spherical particles having a diameter of no more than about 500 nm.

Claim 39 (original): The method of claim 1, wherein the agent is a nonparticulate agent.

Claim 40 (original): The method of claim 1, wherein the fluid is administered at a flow rate of 0.066-960 μl/sec.

Claim 41 (original): The method of claim 1, wherein the fluid is administered at a flow rate of less than 1000 μl/sec.

Claim 42 (original): The method of claim 41, wherein the fluid is administered at a pressure of no more than about 500 mm Hg.

Claim 43 (original): The method of claim 42, wherein the fluid is administered at substantially constant pressure.

Claim 44 (original): The method of claim 43, wherein the organ is non-vascular, and the fluid is administered at a substantially constant pressure of about 5-100 mm Hg.

Claim 45 (original): The method of claim 43, wherein the organ is vascular, and the fluid is administered at a substantially constant pressure of about 5-400 mm Hg.

Claim 46 (original): The method of claim 1, wherein pressure is controlled, and the method further comprises substantially constant monitoring of the pressure during administration of the fluid.

Claim 47 (original): The method of claim 1, further comprising administering a pharmacological substance that improves opening of tight junctions.

Claim 48 (original): The method of claim 1, wherein the organ is a hollow viscus, and the method further comprises partially filling the hollow viscus with an inflatable space occupier before administering the fluid.

Claim 49 (original): The method of claim 1, wherein the pressure is controlled by creating a pressure gradient in a solid portion of the organ, wherein the pressure gradient is preselected to deliver the agent to the predetermined region.

Claim 50 (original): The method of claim 49, wherein the pressure gradient is highest inside the organ.

Claim 51 (original): The method of claim 49, wherein the pressure gradient is highest outside the organ.

Claim 52 (original): A method of determining a threshold pressure for selective administration of a therapeutic or diagnostic substance, the method comprising:

isolating a hollow organ space;

one or more times, introducing a test fluid into the hollow organ space at a preselected flow rate; and

one or more times, administering a test solution to determine a pressure at which leakage across epithelial or endothelial tight junctions occurs; and

administering a liquid including the therapeutic or diagnostic substance by introducing the liquid into the isolated hollow organ space, during which the pressure is not exceeded with the purpose of preferentially delivering the substance to an epithelial layer of the hollow organ space, or during which the peak pressure is exceeded with the purpose of preferentially delivering the substance to a subepithelial layer of the hollow organ space.

Claim 53 (original): The method of claim 52 wherein administering the liquid comprises administering the liquid at a pressure that at least temporarily exceeds the peak pressure, with the purpose of preferentially delivering the substance to the subepithelial or subendothelial layer.

Claim 54 (original): A method of determining the delivery pressure for selective administration of a therapeutic or diagnostic substance, the method comprising:

isolating a hollow organ space;

one or more times, introducing a test fluid into the hollow organ space at a preselected approximately constant pressure;

one or more times, measuring the infusion rate of the administered fluid as the test fluid is introduced; and

administering a liquid including a test solution into the hollow organ space and determining a flow rate at which paracellular leakage across endothelial or epithelial tight junctions occurs.

Claim 55 (original): The method of claim 52 wherein the test fluid has a viscosity substantially similar to that of the liquid containing the therapeutic or diagnostic substance.

Claim 56 (original): The method of claim 52 wherein isolating the hollow organ space comprises introducing a catheter into the hollow organ space, and substantially sealing one or more outlets from the hollow organ space.

Claim 57 (original): A method of delivering a therapeutic or diagnostic substance, the method comprising:

introducing a flexible catheter into an organ lumen lined with polar epithelial cells; and

infusing a therapeutic or diagnostic substance through the catheter into the organ lumen under preselected, controlled pressure conditions at which the therapeutic or diagnostic substance is delivered substantially only to apical surfaces of the epithelial cells and substantially not to any subepithelial regions.

Claim 58 (original): The method of claim 57 wherein the organ lumen is an hepatic or biliary duct and the therapeutic or diagnostic substance is infused at a pressure sufficient to deliver the agent substantially only to cholangiocytes lining the hepatic or biliary duct.

Claim 59 (original): The method of claim 57, further comprising infusing the therapeutic or diagnostic substance into the organ lumen under pre-selected, controlled pressure conditions at which the therapeutic or diagnostic substance is delivered not only to apical surfaces of the epithelial cells but also to subepithelial regions including basal surfaces of the epithelial cells.

Claim 60 (original): The method of claim 59 wherein the body lumen is an hepatic or biliary duct, and the therapeutic or diagnostic substance is infused at a sufficient pressure to deliver the agent to cholangiocytes, hepatocytes, or both.

Claim 61 (original): An access device for targeted delivery of therapeutic or diagnostic agents, the access device comprising:

an elongated cannula having a wall, proximal and distal ends, and a lumen configured to contain a sharp-tipped trochar for penetrating a wall of a desired body organ having a hollow space therein; and

first and second balloons spaced axially along the cannula at positions such that, when the cannula is inserted through the wall of the desired body organ and the balloons are inflated, the first balloon engages an inner face of the organ and the second balloon engages an outer face of the organ, holding the distal end of the cannula in position within the hollow space inside the organ and substantially sealing against leaks.

Claim 62 (original): The access device of claim 61 further comprising a drainage line communicating with a drainage inlet distal to the first and second balloons.

Claim 63 (original): The access device of claim 61 further comprising inflation ports positioned at or near the proximal end of the cannula for inflating the first and second balloons.

Claim 64 (original): The access device of claim 61 further comprising a selectively removable occluder that selectively closes the cannula.

Claim 65 (original): The access device of claim 64 wherein the occluder comprises a cannula cap.

Claim 66 (original): The access device of claim 61 wherein the cannula consists of bio-compatible materials.

Claim 67 (original): The access device of claim 61 further comprising a flexible catheter having an exterior and a distal tip, the catheter being capable of insertion through the cannula, the catheter including an inflatable balloon near its distal tip, that upon inflation is capable of occluding a duct communicating with the desired body organ into which organ the tubular body is introduced.

Claim 68 (original): The access device of claim 67, wherein the catheter comprises multiple lumens, and one of the multiple lumens communicates with the exterior of the catheter proximally of the inflatable balloons.

Claim 69 (original): The access device of claim 67 wherein at least one of the multiple lumens communicates with the exterior of the catheter distally of the inflatable balloon.

Claim 70 (currently amended): A method of accessing an interior of a gall bladder, the method comprising:

inserting a trochar into a cannula having first and second peripheral inflatable cuffs;

introducing the trochar, together with the cannula, at an insertion site through the wall of the gall bladder and advancing the cannula into the gall bladder such that the first inflatable cuff enters the gall bladder but the second inflatable cuff does not;

inflating the first cuff so that it abuts an inner face of the ~~gallbladder~~ gall bladder around the insertion site; and

inflating the second cuff so that it abuts an outer face of the ~~gallbladder~~ gall bladder around the insertion site.

Claim 71 (original): A method of delivering a therapeutic or diagnostic agent to a selected portion of the liver, the method comprising:

introducing a catheter into a hepatic duct draining the selected portion of the liver;

occluding the duct normograde from a distal tip of the catheter; and

infusing the therapeutic or diagnostic agent through the catheter into at least a portion of the selected portion of the liver at a preselected pressure that has been determined to move the agent out of the duct and into the periductular tissue.

Claim 72 (original): The method of claim 71, wherein the hollow gastrointestinal viscus is an hepatobiliary duct, and the periductular tissue is hepatic tissue.

Claim 73 (original): The method of claim 71 wherein the viscus has a vascular flow exiting therefrom, and the method further comprises at least partially occluding the vascular flow exiting from the viscus such that uptake of the agent in the viscus is enhanced.

Claim 74 (original): The method of claim 73, wherein the vascular flow is venous or lymphatic flow.

Claim 75 (original): The method of claim 71, wherein the viscus is at least a portion of at least one of a gallbladder, a pancreas, a liver, a bile duct, an intestine, a stomach, an esophagus, a trachea, a bronchus, a fallopian tube, a uterus, a cervix, a vagina, a duct of a parotid gland, a duct of a salivary gland, a prostate gland, a ureter, a urinary bladder, and a kidney of the patient.

Claim 76 (original): The method of claim 71, further comprising introducing into the viscus a pharmacological substance that tends to open tight junctions between epithelial cells.

Claim 77 (original): A method of introducing a therapeutic or diagnostic agent into a biological structure within the body, comprising introducing the agent into the biological structure in a liquid at a constant pressure.

Claim 78 (original): A method of increasing a size of a body duct or viscus, comprising forming an isolated chamber within the body duct or viscus, and introducing fluid under pressure into the isolated chamber to increase the size.